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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,475	11/19/2001	Jaime E. Ramirez-Vick	25527-0003 C1	6193

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EXAMINER
FORMAN, BETTY J

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 11/06/2002 7

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,475	RAMIREZ-VICK ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☒ Claim(s) *3-9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

1. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Claim Objections

2. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not bc renumbered. When new claims are prcsented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 3-9 been renumbered 4-10.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1-7 are indefinite in Claim 1 for being incomplete in omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: steps of increasing the hybridization rate. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded, *Ex parte Erlich*, 3 USPQ2d 1011 at 6. It is suggested that Claim 1 be amended to recite positive and active method steps e.g. determining rate of hybridization, measuring rate of hybridization, increasing rate of hybridization, etc.

b. Claims 1-7 are indefinite in Claim 1, step f) for the recitation "detecting the hybridized target" because hybridization lacks proper antecedent basis in the claim. It is suggested that Claim 1 be amended to provide proper antecedent basis e.g. in step c) replace "contacting" with "hybridizing" and insert "the probe nucleic acids attached to" before "the solid support".

c. Claim 8 is indefinite in the recitation "at least one member of a complementary pair" because the recitation lacks proper antecedent basis in Claim 1. It is suggested that the claim be amended to provide proper antecedent basis e.g. replace "at least one member of a complementary pair" with "said probe nucleic acid molecule or said nucleic acid target molecule".

d. Claims 9-15 are indefinite in Claim 9 for being incomplete in omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: steps of increasing the hybridization rate. Method claims need not recite all operating details but should at least recite positive, active steps so that the claims will set out and

circumscribe a particular area with a reasonable degree of precision and particularity and make clear what subject matter that claims encompass as well as make clear the subject matter from which others would be precluded, *Ex parte Erlich*, 3 USPQ2d 1011 at 6. It is suggested that Claim 9 be amended to recite positive and active method steps e.g. determining rate of hybridization, measuring rate of hybridization, increasing rate of hybridization, etc.

e. Claims 9-16 are indefinite in Claim 9, step f) for the recitation "detecting the hybridized target" because hybridization lacks proper antecedent basis in the claim. It is suggested that Claim 9 be amended to provide proper antecedent basis e.g. in step c) replace "contacting" with "hybridizing" and insert "the probe nucleic acids attached to" before "the solid support".

f. Claim 16 is indefinite in the recitation "at least one member of a complementary pair" becausc the recitation lacks proper antecedent basis in Claim 9. It is suggested that the claim be amended to provide proper antecedent basis e.g. replace "at least one member of a complementary pair" with "said probe nucleic acid molecule or said nucleic acid target molecule".

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 1-3, 6, 7, 9-11, 13 and 14 are rejected under 35 U.S.C. 102(e) as being anticipated by Baselt (U.S. Patent No. 5,981,297, filed 5 February 1997).

The claims are drawn to a method for increasing the hybridization rate of nucleic acids in a nucleic acid assay. Examiner's interpretation of the claim does not give patentable weight to the preamble of the claim because the method steps do not recite a steps of increasing hybridization rate, measuring hybridization rate, determining hybridization rate or comparing hybridization rate and as such there is no relationship between the method and the recited purposed for the method i.e. increasing the hybridization rate. The courts have stated that the preamble is non-limiting where it merely recites the purpose of a process which is fully set forth in the body of the claim (see *in re Hiaro* 535 F2d 67, 70, 190 USPQ 15, 16-17 (CC)A 1976).

Regarding Claim 1, Baselt discloses a method of nucleic acid hybridization comprising: attaching probe nucleic acid molecules of known sequence (i.e. binding molecules capable of undergoing selective binding with a target species, Column 4, lines 20-24)to a solid support; labeling nucleic acid target molecules with paramagnetic labels; contacting the labeled target molecules with the solid support; activating a magnetic field whereby the labeled molecules are attracted to the solid support (Column 7, lines 21-37); washing the support and inverting the polarity of the magnetic field to remove any unbound or non-specifically bound molecules; and detecting the hybridized target nucleic acid molecules (Column 3, line 39-Column 4, line 8 and Column 7, lines 21-64) wherein the method operates faster than other techniques (Column

4,lines 35-38). Therefore, the method of Baselt et al increases the rate of hybridization as claimed.

Regarding Claim 2, Baselt et al disclose the solid support is silicon (Column 6, lines 32-36).

Regarding Claim 3, Baselt et al disclose the solid support is coated with gold (Column 6, lines 47-50).

Regarding Claim 6, Baselt et al disclose the paramagnetic labels are attached to the nucleic acid molecules using cleavable conjugating molecules i.e. selective binding molecules (Column 4, lines 23-28).

Regarding Claim 7, Baselt et al disclose the nucleic acid molecules are oligonucleotides or DNA (Column 4, lines 3-5).

Regarding Claim 9, Baselt disclose a method of nucleic acid hybridization comprising: attaching probe nucleic acid molecules to a solid support; labeling nucleic acid target molecules of known sequence (i.e. target species capable of selective binding, Column 4, lines 20-24) with paramagnetic labels; contacting the labeled target molecules with the solid support; activating a magnetic field whereby the labeled molecules are attracted to the solid support (Column 7, lines 21-37); washing the support and inverting the polarity of the magnetic field to remove any unbound or non-specifically bound molecules; and detecting the hybridized target nucleic acid molecules (Column 3, line 39-Column 4, line 8 and Column 7, lines 21-64) wherein the method operates faster than other techniques (Column 4,lines 35-38). Therefore, the method of Baselt et al increases the rate of hybridization as claimed.

Regarding Claim 10, Baselt et al disclose the solid support is silicon (Column 6, lines 32-36).

Regarding Claim 11, Baselt et al disclose the solid support is coated with gold (Column 6, lines 47-50).

Regarding Claim 13, Baselt et al disclose the paramagnetic labels are attached to the nucleic acid molecules using cleavable conjugating molecules i.e. selective binding molecules (Column 4, lines 23-28).

Regarding Claim 14, Baselt ct al disclose the nucleic acid molecules are oligonucleotides or DNA (Column 4, lines 3-5).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 4, 8, 12 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Baselt (U.S. Patent No. 5,981,297, filed 5 February 1997) in view of Kausch et al. (U.S. Patent No. 5,665,582, filed 18 April 1994).

Regarding Claims 4 and 12, Baselt teaches a method of nucleic acid hybridization comprising: attaching probe nucleic acid molecules of known sequence to a solid support; labeling nucleic acid target molecules with paramagnetic labels; and contacting the labeled target molecules with the solid support (Column 3, line 39-Column 4, line 8) wherein the paramagnetic labels comprising particles having a diameter of from 1 to 5 μm (Column 6, lines 63-67) but Baselt does not teach a diameter of 1 to 10 nm. However, Kausch et al. teach a similar method of nucleic acid hybridization comprising attaching nucleic acid molecules to a

solid support; labeling nucleic acid molecules with paramagnetic labels; and contacting the labeled molecules with the solid support (column 5, lines 36-55) wherein the paramagnetic labels comprising particles having a diameter of from 1 to 10 nm wherein the preferred diameter provides for faster binding reaction and the particles do not inter-aggregate and are easy to sterilize (Column 23, lines 53-67). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the paramagnetic labels of Baselt by using the smaller paramagnetic labels taught by Kausch et al. for the expected benefits of faster binding reaction, inter-aggregation prevention, and easy of sterilization as taught by Kausch (Column 23, lines 53-67).

Regarding Claims 8 and 16, Baselt teaches the nucleic acid molecules are labeled (Column 3, lines 48-51) but Baselt does not teach one member of a complementary pair is labeled with a fluorescent detection molecule. However, Kausch et al. teach the similar method wherein at least one member of a complementary pair is labeled with a fluorescent detection molecule (Column 6, lines 16-26). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to label at least one member of a complementary pair with a fluorescent detection molecule in the method of Baselt for the obvious benefit of detecting the bound molecules simply via fluorescent microscope as taught by Kausch et al. (Column 6, lines 21-23).

9. Claims 5 and 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Baselt (U.S. Patent No. 5,981,297, filed 5 February 1997) in view of Roelant (U.S. Patent No. 6,001,573, filed 23 October 1997).

Regarding Claims 5 and 13, Baselt teaches a method of nucleic acid hybridization comprising: attaching probe nucleic acid molecules of known sequence to a solid support;

labeling nucleic acid target molecules with paramagnetic labels; and contacting the labeled target molecules with the solid support (Column 3, line 39-Column 4, line 8) but Baselt does not teach the paramagnetic labels comprise paramagnet porphyrins. Roelant teach a similar method of nucleic acid hybridization comprising attaching probe molecules to a solid support; labeling target molecules with paramagnetic labels; contacting the labeled molecules with the solid support; and detecting the hybridized target molecules wherein the paramagnetic labels comprise paramagnetic porphyrins (Column 5, line 66-Column 6, line 16) wherein the porphyrin label provides a universal label which attaches irreversibly without bridging agents and can be detected in an amount which is proportional to the number of labeled particles (Column 3, lines 59-65). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to label the paramagnetic beads of Baselt with the porphyrin label taught by Roelant for the expected benefit of irreversible attachment of the label and for the additional benefit of quantifying target simply by quantifying the label as taught by Roelant (Column 3, lines 59-65).

10. Claims 1, 2, 4, 6-10, 12 and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kausch et al. (U.S. Patent No. 5,665,582, filed 18 April 1994).

The claims are drawn to a method for increasing the hybridization rate of nucleic acids in a nucleic acid assay. Examiner's interpretation of the claim does not give patentable weight to the preamble of the claim because the method steps do not recite a steps of increasing hybridization rate, measuring hybridization rate, determining hybridization rate or comparing

hybridization rate and as such there is no relationship between the method and recited purpose for the method i.e. increasing the hybridization rate. The courts have stated that the preamble is non-limiting where it merely recites the purpose of a process which is fully set forth in the body of the claim (see *in re Hiaro* 535 F2d 67, 70, 190 USPQ 15, 16-17 (CC)A 1976).

Regarding Claims 1 and 9, Kausch et al. teach a method of nucleic acid hybridization comprising: attaching nucleic acid target molecules to a solid support; labeling nucleic acid molecules of known sequence with paramagnetic labels; contacting the support with the labeled nucleic acid molecules of know sequence; washing the support to remove any unbound or non-specifically bound molecules; and detecting the hybridized target nucleic acid molecules (Column 9, line 57-Column 10, line 8) wherein the attracting (i.e. binding) is via a magnetic field (i.e. magnetic means) (Column 5, lines 50-51) and wherein the polarity is reversed (i.e. the magnet is removed to wash and remove unbound or non-specifically bound molecules (Fig. 11) but they do not teach activating a magnetic field whereby the labeled molecules are attracted to the solid support. However, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to activate the magnetic field of Kausch et al. to attract the target molecules to the solid support for the obvious benefit of localizing target molecules to a specific area on the solid support.

Regarding Claims 2 and 10, Kausch et al. teach the solid support is glass (Column 12, lines 14-16).

Regarding Claims 4 and 12, Kausch et al. teach the paramagnetic labels comprising particles having a diameter of from 1 to 10 nm (Column 23, lines 53-67).

Regarding Claims 6 and 14, Kausch et al. teach the paramagnetic labels are attached to the nucleic acid molecules using cleavable conjugating molecules i.e. biotin-streptavidin (Column 39, lines 20-26).

Regarding Claims 7 and 15, Kausch et al. teach the nucleic acid molecules are oligonucleotides, genomic DNA, RNA or fragments thereof (Column 5, lines 37-45 and 58-66).

Regarding Claims 8 and 16, Kausch et al. teach at least one member of a complementary pair is labeled with a fluorescent detection molecule (Column 6, lines 16-26).

11. Claims 3 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kausch et al. (U.S. Patent No. 5,665,582, filed 18 April 1994) as applied to claims 1 and 9 above, and further in view of Baselt (U.S. Patent No. 5,981,297, filed 5 February 1997)

Regarding Claim 11, Kausch et al. teach a method of nucleic acid hybridization comprising: attaching nucleic acid target molecules to a solid support; labeling nucleic acid molecules of known sequence with paramagnetic labels; contacting the support with the labeled nucleic acid molecules; and detecting the hybridized target nucleic acid molecules (Column 9, line 57-Column 10, line 8) but they do not teach the solid support is or is coated with a metal. However, Baselt teaches a similar method the solid support is coated with gold (Column 6, lines 47-50). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to coat the support of Kausch et al. with gold as taught by Baselt for the expected benefit of providing a means on the support for carrying voltage to thereby regulate magnetic fields as taught by Baselt (Column 8, lines 49-67).

12. Claims 5 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kausch et al. (U.S. Patent No. 5,665,582, filed 18 April 1994) as applied to claims 1 and 9 above and further in view of Roelant (U.S. Patent No. 6,001,573, filed 23 October 1997).

Regarding Claim 13, Kausch et al. teach a method of nucleic acid hybridization comprising: attaching nucleic acid target molecules to a solid support; labeling nucleic acid

molecules of known sequence with paramagnetic labels; contacting the support with the labeled nucleic acid molecules; and detecting the hybridized target nucleic acid molecules (Column 9, line 57-Column 10, line 8) but they do not teach the paramagnetic labels comprise paramagnetic porphyrins. Roelant teach a similar method of nucleic acid hybridization comprising attaching probe molecules to a solid support; labeling target molecules with paramagnetic labels; contacting the labeled molecules with the solid support; and detecting the hybridized target molecules wherein the paramagnetic labels comprise paramagnetic porphyrins (Column 5, line 66-Column 6, line 16) wherein the porphyrin label provides a universal label which is attached irreversibly without bridging agents and is detected in an amount which is proportional to the number of labeled particles (Column 3, lines 59-65). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to label the paramagnetic beads of Kausch et al. with the porphyrin label taught by Roelant for the expected benefit of irreversible attachment of the label and for the additional benefit of quantifying target simply by quantifying the label as taught by Roelant (Column 3, lines 59-65).

Prior Art

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure:

Lee et al. (U.S. Patent No. 5,807,758, issued 15 September 1998) teach a method of nucleic acid hybridization comprising: attaching probe nucleic acid molecules to a solid support; labeling nucleic acid target molecules with paramagnetic labels; contacting the labeled

target molecules with the solid support; and detecting the target nucleic acid molecules (Column 4, line 11-Column 5, line 32).

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
October 31, 2002